REMARKS

Applicants thank the Examiner for rejoining and examining the claims in Groups I, II and III of the previous Restriction Requirement.

I. Amendments to the Specification:

Paragraphs 25-30 of the specification have been amended to define the numbers shown in the figures. Support for these amendments can be found throughout the specification as filed, for example, in paragraphs 40-43, 47-49, 53-54, 68-70 and 74.

II. Amendments to the Claims:

Claims 3-5 and 23 have been canceled. Claim 1 has been amended to define the claimed scaffolded fusion polypeptides as soluble, and to define each functional domain as comprising the amino acid sequence of a soluble loop or strand of an integral membrane protein. Claim 1 has been amended further to define each scaffold domain as comprising two soluble scaffold strands, wherein one scaffold strand comprises the amino acid sequence of SEQ ID NO:6 and the other scaffold strand comprises the amino acid sequence of SEQ ID NO:7, and wherein the scaffolded fusion polypeptide binds an antibody that recognizes the native, properly folded form of said integral membrane protein but not linear fragments of said integral membrane protein. Support for these amendments can be found throughout the specification as filed, for example, at paragraphs 7-10, 22, 44, 61, and 154-156. New claims 26-31 have been added to capture additional embodiments of the claimed subject matter. Support for these new claims can be found throughout the specification as filed, for example, at paragraphs 78, 148, 83, 141-146, 102, 153-155, 107-109 and in Table 3. No new matter has been added.

Upon entry of these amendments, claims 1, 2, 6-9, 17, 22 and 24-31 will be pending.

III. Drawings

The drawings have been objected to for including numbers that are not mentioned in the "Brief Description of Figures" in the specification. Applicants have amended paragraphs 25-30 of the specification to add descriptions of the numbers to the description of each figure. In view of these amendments, Applicants submit that the drawings now

comply with 37 CFR 1.84(p)(5), and respectfully request the reconsideration and withdrawal of this objection.

IV. Claim Objections

Claims 9 and 25 are objected to for depending upon rejected base claim 2. Applicants believe that claims 1 and 2 are allowable and therefore the objection should be withdrawn. Furthermore, new independent claim 26 (and claim 27 which depends therefrom) are similar to claims 9 and 25 and thus should be allowable. Applicants, therefore, respectfully request that this objection be reconsidered and withdrawn.

V. Claim Rejections Under 35 USC §112

A. Enablement

Claims 1-8 and 22-24 have been rejected as allegedly lacking enablement over their entire scope. In section 8 on page 4 of the Office Action dated November 21, 2003, the Examiner states, "the specification, while being enabling for a scaffolded fusion polypeptide comprising SEQ ID NO:10 and SEQ ID NO:31, does not reasonably provide enablement for any other scaffolded fusion polypeptide." More specifically, in section 9 on page 4 the Examiner states,

> The language of said claims encompasses a massive genus of functional domains flanked by scaffolds with no explicit delineation of the fusion polypeptide itself. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to **make** or **use** the invention commensurate in scope with these claims.

Emphasis in original. Applicants respectfully disagree and traverse this rejection.

Applicants respectfully maintain that the above listed claims were fully enabled. Nevertheless, claims 3-5 and 23 have been canceled, and claim 1 has been amended. This rejection appears to be based on several separate aspects of enablement which are of concern to the Examiner. These will be discussed individually below.

The Examiner is concerned that it is unclear which zinc finger motifs work in the invention as claimed. *See* Office Action mailed November 21, 2003 at section 14 on page 6. The subject claims have been amended to recite the use of only one particular zinc finger motif, that involving SEQ ID NOS: 6 and 7. The efficacy of this motif was demonstrated in the specification in the form of two exemplified scaffolded fusion

polypeptides involving CCR5 sequences, which successfully employed the zinc finger motif of SEQ ID NOS:6 and 7 at three different locations within each polypeptide. The exemplified polypeptides were competent in binding two particular antibodies known to bind conformational epitopes of CCR5. Thus, the Examiner's concern regarding the selection of an appropriate zinc finger motif has been alleviated.

Relatedly, the Examiner is concerned that the inclusion of one or more zinc finger motifs may not render the claimed scaffolded fusion polypeptide soluble. *See* section 16 at page 7 of the Office Action of November 21, 2003. However, the subject claims have been amended to recite that the scaffolded fusion polypeptide is soluble. The skilled practitioner could readily determine whether a given scaffolded fusion polypeptide is soluble by very simple and routine experimentation. This is believed to obviate the Examiner's concern regarding solubility of the claimed polypeptides.

Another concern is the allegedly unpredictable nature of selecting functional domains and flanking scaffold domains "to insure that the scaffolded fusion polypeptide so constructed would have the desired activity." See Office Action of November 23, 2003 at section 11 on page 5. The selection of scaffold domains has been addressed above. Indeed, since the zinc binding aspect of the scaffold domains has been specified in the amended claims, this aspect of making and using a scaffolded fusion polypeptide is quite predictable. The selection of functional domains is also predictable based on the subject claims as amended. The only biological activity required by the claims is that the scaffolded fusion polypeptide binds an antibody that recognizes the native, properly folded form of the integral membrane protein from which a functional domain was obtained. This is readily ascertainable by the skilled practitioner, who can routinely determine antibody binding to the native, properly folded integral membrane protein as well as to any particular scaffolded fusion polypeptide.

A final concern is that it is allegedly unclear how many transmembrane domains of a G-protein coupled receptor are required for function, given that Ling et al. teach that only five transmembrane domains are required for CCR5 to function. *See* Office Action of November 21, 2003 at section 17 on page 7. Because the claims only require antibody binding by way of function, the Ling et al. reference is believed to be irrelevant, as that publication dealt with chemokine receptor function.

Based on above amendments and comments, Applicants submit that the claimed invention is fully enabled in the specification, and respectfully request the reconsideration and withdrawal of this rejection.

B. Claims 1-8, 17, and 22-24- written description

Claims 1-8 and 22-24 have been rejected for allegedly lacking written description in the specification. Specifically, it is stated in section 21 on page 8 of the Office Action dated November 21, 2003 that "The claims do not require that the 'functional polypeptide' to possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity." It is further stated on page 9 of the Office Action, "Further, Laity *et al.* ... teach that zinc binding domains exhibit great structural and functional diversity (pp.39) thus requiring a greater, more detailed disclosure in the instant Specification to support the written description requirement." Applicants respectfully disagree and traverse.

Applicants respectfully maintain that the above listed claims were fully described in the specification in such a way as to reasonably convey to one skilled in the art that Applicants, at the time of filing, had possession of the claimed invention. However, solely in the interest of facilitating prosecution, claims 3-5 and 23 have been canceled and claim 1 has been amended. Applicants submit that the claims as amended are clearly defined as having particular structures (*i.e.*, soluble loops or strands of native integral membrane proteins and scaffold domains comprising SEQ ID NOs: 6 and 7) and specific activities (*i.e.*, binding an antibody that specifically recognizes the native, properly folded form of the corresponding integral membrane protein), all of which are fully described in the specification as filed. Furthermore, the Federal Circuit recently re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed,'" *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). While the applicant must "blaze marks on trees," rather than "simply [provide] the public with a forest of trees," an Applicant is not required to explicitly describe each of the trees in the forest. *See Unocal*, 208 F.3d at 1000. The Court emphasized the importance of what the person of ordinary skill in the art would

understand from reading the specification, rather than whether the specific embodiments had been explicitly described or exemplified. Indeed, as the court noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Unocal*, 208 F.3d at 1001 (emphasis added).

Accordingly, one skilled in the art, knowledgeable of integral membrane proteins and the soluble and transmembrane domains that they possess, enlightened by teachings of the present application (particularly, for example, the zinc binding motifs defined by SEQ ID NOs:6 and 7), could readily envision countless scaffolded fusion polypeptides designed by fusing the known soluble extracellular loops of an integral membrane protein to scaffold domains comprising SEQ ID NOs: 6 and 7. Applicants submit that, from reading the specification, the skilled person would immediately recognize that, at the time the specification was filed, the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563); namely, a genus of soluble scaffolded fusion polypeptides comprising soluble loops or strands of an integral membrane protein fused to scaffold domains comprising SEQ ID NOs: 6 and 7, wherein the scaffolded fusion polypeptide binds an antibody that recognizes the native, properly folded form of said integral membrane protein but not linear fragments of said integral membrane protein. Therefore, the specification contains an adequate written description of the claimed polypeptides.

For the above reasons, Applicants respectfully assert that the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Therefore, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants believe that this application is now in condition for allowance.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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